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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/930,915	08/15/2001	Ashley J. Birkett	ICC-102.2US 81175	2278
24628	7590	02/23/2007		
WELSH & KATZ, LTD 120 S RIVERSIDE PLAZA 22ND FLOOR CHICAGO, IL 60606			EXAMINER PENG, BO	
			ART UNIT	PAPER NUMBER
			1648	
SHORTENED STATUTORY PERIOD OF RESPONSE		MAIL DATE	DELIVERY MODE	
3 MONTHS		02/23/2007	PAPER	

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.		Applicant(s)	
	09/930,915		BIRKETT, ASHLEY J.	
	Examiner		Art Unit	
	Bo Peng		1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 November 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9, 12-17, 19-33, 35-38 and 42-78 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9, 12-17, 19-33, 35-38 and 42-78 is/are rejected.
- 7) ☒ Claim(s) 12-14, 17, 27-29, 36, 59-62 and 76 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>11/22/06:10/10/06</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 22, 2006 has been entered.
2. This Office Action is in response to the amendment filed September 21, 2006. Claims 1-9, 12-17, 19-33, 35-38 and 42-78 are pending, and are under consideration in this Office action.

Information Disclosure Statement

3. Applicant's IDS form 1449 submitted on November 22, 2006 has been considered by the examiner. The initialed and dated copy of IDS form 1449 is attached to the instant Office action.
4. The information disclosure statements filed on October 10, 2006 fails to completely comply with 37 CFR 1.98(b)(5) because they lack titles of the publications listed under other documents (See MPEP 609). The information referred to therein has not been considered. The US and foreign patent documents have been considered.

Claim Rejections - 35 USC § 112, first paragraph

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person

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skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. The rejection of Claims 1-9, 12-17, 19-33, 35-38 and 42-78 under 35 U.S.C. § 112, first paragraph, for lacking scope of enablement, **is withdrawn** in view of the amendment to the claims.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. The rejection of Claims 12-14, 17, 27-29, 36, 37, 59-62 and 76 under 35 U.S.C. 103(a), as being unpatentable over Pumpens et al. (1995) in view of Zlotnick et al (1997), **is withdrawn** in view of Applicant's argument.

9. The rejection of Claims 1-9, 15, 16, 18-26, 30-33, 35, 38, 42-58, 63-75, 77 and 78 under 35 U.S.C. 103(a), as being unpatentable over Pumpens et al. (1995) in view of Zlotnick et al (1997), **is maintained** for the reasons of record.

10. Applicant argues again that Pumpens' constructs have no stabilization at the C-terminus of an HBcΔ, Zlotnick has neither an insert epitope in his construct, nor a suggestion of where to

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put one; and neither reference teaches what to do about the non-conservative substitutions present in Zlotnick. This argument has been considered and addressed in the previous Office action of record (see Final rejection, Paragraph 15 and 17-24).

11. Applicant also argues that Ulrich, as ordinary skill in the art, who stated that the stability problem of HBc was not solved, did not suggest that the desired stability could be achieved by combining teachings of both Pumpens and Zlotnick, but rather maintained that the problem still had to be solved (Remarks, Paragraph 2, p. 32).

12. Applicant's argument is not relevant even though Ulrich did not combine teachings of both Pumpens and Zlotnick. The knowledge of Pumpen and Zlotnick are still suggestive to those of ordinary skill in the art. In the instant claims, specifically, all basic structural feature limitations are taught or suggested by Pumpens and Zlotnick. Applicant has not explicitly pointed out which specific structures of the alleged HBc chimera are different from the prior art result in enhancing the stability of the alleged HBc chimera. Therefore, the instant Claims 12-14, 17, 27-29, 36, 27, 59-62 and 76 are obvious over Pumpens et al. (1995) in view of Zlotnick et al (1997).

13. The following are new rejections:

Claim Rejections - 35 USC § 112, first paragraph

14. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which

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it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. Claims 18-38 and 42-78 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection affects all dependent claims.

16. Please note that the newly amended scope of “in which no more than about ~~40~~ 5 percent the amino acid residues are conservatively substituted in the HBc sequence of the chimera as compared to a sequence of SEQ ID NO: 246-251 from position 1 through 149 ” in Claims 18, 42 and 63 is NEW MATTER. No description of “5 percent the amino acid residues are conservatively substituted in the HBc sequence of the chimera as compared to a sequence of SEQ ID NO: 246-251 from position 1 through 149 ” is found in the specification.

17. Removal of all new matter is required. *In re Russsmussen* 210 USPQ 325.

Claim Rejections - 35 USC § 103

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

19. Claims 12-14, 17, 27-29, 36, 37, 59-62 and 76 are rejected under 35 U.S.C. 103(a), as being unpatentable over Pumpens et al. (1995), in view of Zlotnick et al (1997) as applied to

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Claims 1-9, 15, 16, 18-26, 30-33, 35, 38, 42-58, 63-75, 77 and 78, further in view of Thornton et al. (US 5,143,726, cited in IDS).

20. Claims 12-14, 17, 27-29, 36, 37, 59-62 and 76 are directed to an immunogenic HBc chimera, **wherein said chimera contains a heterologous linker residue for a conjugated epitope**, wherein said heterologous linker residue for a conjugated epitope is peptide-bonded at a position in the HBc sequence between amino acid residues 76 and 85, and at least 4 residues of the HBc sequence of positions 76 through 85 are present, wherein the HBc sequence between amino acid residues 76 and 85 is present, but interrupted by said heterologous linker residue for a conjugated epitope, wherein said heterologous linker residue for a conjugated epitope is selected from the group consisting of a **lysine**, aspartic acid, glutamic acid, **cysteine** and a tyrosine residue, wherein said heterologous linker residue for a conjugated epitope or a heterologous epitope is a heterologous epitope, wherein said heterologous epitope comprises up to about 245 amino acid residues, wherein said heterologous epitope is a B cell epitope.

21. Pumpens (1995) teaches immunogenic compositions and vaccines using recombinant HBc chimera molecules of a variety of lengths up to about 380 or 600 amino acid residues in length. Pumpens teaches that both full-length HBc and C-terminal truncated HBc Δ can form capsid particles. The HBc and HBc Δ chimeras can carry B-cell and T-cell epitopes at their N-terminal, C-terminal or at internal immunodominant loop sites at positions 76 through 85 (See Figure 1 and Tables 1 through 3). Pumpens also teaches such chimeras can contain two epitopes at both the immunodominant loop and C-terminal (see Table 2). Pumpens discloses that HBc chimeras with C-terminal truncations are capable of self-assembly and do not bind or 'pack' nucleic acids in their capsid particles (page 67, col. 1).

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22. Zlotnick teaches recombinant C-terminal deleted HBc (HBc Δ) molecules that are capable of assembling into capsids and do not pack viral RNA within their capsids. Zlotnick teaches that an addition of Cys at C-terminus of HBc Δ can enhance stability of HBc Δ (p. 9558).

23. Thornton teaches the use of HBc as an immunogenic carrier molecule where a polypeptide is linked to the carrier/core molecule through an amino acid side chain on the core molecule (see abstract, Columns 9 and 10, and Line 5-14, Column 21). Thornton teaches that operatively linking a polypeptide immunogen to HBcAg particle increases the immunogenicity of the linked immunogen to an unexpected degree through the operation of HBcAg's previously unknown T cell dependent and T cell independent determinants. Thornton teaches that methods for operatively linking individual polypeptides through an amino acid residue side chain to form an immunogenic conjugate, i.e., a branched-chain polypeptide polymer, are well known in the art (Line 13-45, column 10). Useful side chain functional groups include epsilon-amino groups, beta- or gamma-carboxyl groups, thiol (--SH) groups and aromatic rings (e.g. **tyrosine** and **histidine**). Furthermore, Thornton teaches that, as is well known in the art, both the HBcAg protein and polypeptide immunogen can be used in their native form or their functional group content may be modified by succinylation of **lysine** residues or reaction with **cysteine**-thiolactone. The polypeptides can also be modified to incorporate spacer arms, such as hexamethylene diamine or other bifunctional molecules of similar size, to facilitate linking (Line 13-45, column 10).

24. One of ordinary skill in the art would have been motivated to combine the teachings of Thornton with that of Pumpens and Zlotnick in order to make a HBc Δ molecule that could present an epitope via a side-chain. One would have been motivated to do so, given the

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suggestion by Thornton that operatively linking a polypeptide immunogen to HBcAg particle increases the immunogenicity of the polypeptide, and given the teaching by Zlotnick that HBcΔ with additional Cys at its C-terminus have greatly enhances the stability and does not pack viral RNA into the particles. There would have been a reasonable expectation of success, given the knowledge that both HBc and HBcΔ have been successfully used for displaying heterologous epitopes at their N-, and C-terminals, and immunodominant loop at positions 76 through 85, as taught by Penmpens and Thornton, and given the knowledge that methods for operatively linking individual polypeptides through an amino acid residue side chain to form an immunogenic conjugate are well known in the art, as taught by Thornton. Therefore the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

25. No claims are allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bo Peng, Ph.D. whose telephone number is 571-272-5542. The examiner can normally be reached on M-F, 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, Ph.D. can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Bo Peng, Ph.D.
2/15/07



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